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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,594	09/29/2003	Lars T. Hellman	10223-006007	2642

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FISH & RICHARDSON P.C.
3300 DAIN RAUSCHER PLAZA
60 SOUTH SIXTH STREET
MINNEAPOLIS, MN 55402

EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/673,594	HELLMAN, LARS T.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *9/23/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/30/04; 8/6/04; 10/28/03*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 25-28 are pending and are being acted upon in this Office Action.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 25-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a polypeptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 (as shown in Figure 1), SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 10 as shown in Figure 2A-B and (2) a polypeptide consisting of the N-terminal polyhistidine sequence followed by an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH2 domain, a rat CH3 domain, an opossum IgE CH4 domain and a C-terminal polyhistidine sequence, **does not** reasonably provide enablement for any polypeptide "comprising" at least any two CH3 IgE domains, and a any CH4 IgE domain, wherein said CH4 IgE is heterologous to at least one of said CH3 IgE domains, (2) any polypeptide "comprising" at least two rat CH3 IgE domains or at least two human CH3 IgE domains and any CH4 IgE domain, and (3) any polypeptide "comprising" at least any two CH3 IgE domains, and an opossum CH4 IgE domain, wherein said CH4 IgE is heterologous to at least one of said CH3 IgE domains as set forth in claims 25-28. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a polypeptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 (as shown in Figure 1), SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 10 as shown in Figure 2A-B. The specification further discloses a polypeptide consisting of the N-terminal polyhistidine sequence followed by an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH2 domain, a rat CH3 domain, an opossum IgE CH4 domain and a C-terminal polyhistidine sequence wherein the CH2 and CH4 domains of the polypeptide stabilizes a functional conformation of the CH3 domain.

The specification does not teach how to make all polypeptide as set forth in claims 25-28 because there is insufficient guidance as to the structure of the polypeptide without the amino acid sequence. Further, the term "comprising" is open-ended. It expands the "polypeptide" to include additional amino acids at either or both ends. There is insufficient guidance as to which undisclosed amino acids are to be included and whether the resulting polypeptide maintains a functional conformation of the self IgE CH3 domain, in turn, the polypeptide induces anti-self IgE antibody as a vaccine. Given the unlimited number of polypeptide comprising any CH3 IgE domains so long the polypeptide contains at least two CH3 domains, any CH4 IgE domain in any order, there is insufficient in vivo working demonstrating that any polypeptide is effective for inducing anti-self IgE antibodies as a vaccine.

Nechansky *et al*, PTO 1449, teach that "although it was shown that Cε3 is the region exclusively involved in the interaction with FcεRI, the synthesis of a recombinant single Cε3 domain still being able to bind to FcεRI with high affinity has *never* been successful" (See page 296, col. 1, first paragraph, in particular). In fact, the specification on page 17-18 discloses that the CH2 and CH4 domains serve to promote and stabilize the immunogenic polypeptide such that the specific anti-self IgE response is induced. However, the conformational requirements such as natural folding or stability of IgE polypeptide have made it difficult to generate antibodies that recognize native IgE because the CH3 and CH4 domains within the claimed polypeptide can be any order. It is unpredictable which polypeptide comprising any CH4 IgE domain followed by any CH3 IgE domain followed by any CH3 IgE domain or a polypeptide comprising any CH3 IgE domain followed by any CH4 IgE domain followed by any CH3 IgE domain would maintain secondary structure of the IgE Fc, in turn would induce anti-self IgE response specifically to the CH3 domain.

Further, there are more than 270 living species of non-placental mammals and placental mammals. There is insufficient guidance as to the structure of IgE sequence of all non-placental mammal and placental mammals, much less about the specific IgE domains.

Abaza *et al*, PTO 1449, teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with antibody against the site (See abstract, in particular). Without the amino acid sequence, it is unpredictable which undisclosed immunogenic polypeptide would be useful as a vaccine for inducing anti-human IgE response in humans or anti-self IgE immune response in any animal.

Lederman et al, PTO 1449, teach that a single amino acid substitution in a common African allele of the CD4 molecule ablates binding of the monoclonal antibody IKT4 to said molecule.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

4. Claims 25-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of *all* polypeptide as set forth in claims 25-28 wherein the CH3 and CH4 domains are in any order for inducing anti-self IgE response in any mammal.

The specification discloses only a polypeptide consisting of the amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 (as shown in Figure 1), SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and SEQ ID NO: 10 as shown in Figure 2A-B. The specification

further discloses a polypeptide consisting of the N-terminal polyhistidine sequence followed by an opossum IgE CH2 domain, a rat IgE CH3 domain, an opossum IgE CH2 domain, a rat CH3 domain, an opossum IgE CH4 domain and a C-terminal polyhistidine sequence wherein the CH2 and CH4 domains of the polypeptide stabilizes a functional conformation of the CH3 domain.

Other than the specific polypeptide mentioned above, there is inadequate written description about the structure associated with function of all polypeptide without the amino acid sequence. Further, the term "comprising" is open-ended. It expands the "polypeptide" to include additional amino acids at either or both ends. There is insufficient written description about the amino acids are to be added and whether the resulting polypeptide maintains a functional conformation of the self IgE CH3 domain, in turn, the polypeptide induces anti-self IgE antibody as a vaccine. Adequate written description requires more than a mere statement that it is part of the invention. The amino acid sequence itself is required. The specification provides neither a representative number of polypeptide to describe the claimed genus, nor does it provides a description of structural features that are common to all IgE CH3 domains and all IgE CH4 domains. Without the amino acid sequence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed polypeptide look like.

The specification discloses only polypeptide consisting of IgE CH2-CH3-CH4 domains from opossum, rat, human, and mouse, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of compound to describe the genus for the claimed polypeptide. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone

are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

7. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
November 23, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600